

Full wwPDB X-ray Structure Validation Report (i)

May 14, 2020 – 06:58 pm BST

PDB ID	:	4HW4
Title	:	Discovery of potent Mcl-1 inhibitors using fragment-based methods and
		structure-based design
Authors	:	Friberg, A.; Zhao, B.
Deposited on		
$\operatorname{Resolution}$:	1.53 Å(reported)

This is a Full wwPDB X-ray Structure Validation Report for a publicly released PDB entry.

We welcome your comments at validation@mail.wwpdb.org A user guide is available at https://www.wwpdb.org/validation/2017/XrayValidationReportHelp with specific help available everywhere you see the (i) symbol.

The following versions of software and data (see references (1)) were used in the production of this report:

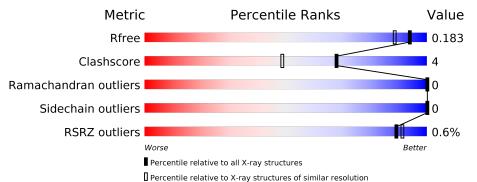
MolProbity	:	4.02b-467
Mogul	:	1.8.5 (274361), CSD as541be (2020)
Xtriage (Phenix)	:	1.13
EDS	:	2.11
Percentile statistics	:	20191225.v01 (using entries in the PDB archive December 25th 2019)
Refmac	:	5.8.0158
CCP4	:	7.0.044 (Gargrove)
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP)	:	2.11

1 Overall quality at a glance (i)

The following experimental techniques were used to determine the structure: X-RAY DIFFRACTION

The reported resolution of this entry is 1.53 Å.

Percentile scores (ranging between 0-100) for global validation metrics of the entry are shown in the following graphic. The table shows the number of entries on which the scores are based.



Metric	$egin{array}{c} { m Whole \ archive} \ (\#{ m Entries}) \end{array}$	${f Similar\ resolution}\ (\#{ m Entries},{ m resolution\ range}({ m \AA}))$
R _{free}	130704	2556 (1.56-1.52)
Clashscore	141614	2634(1.56-1.52)
Ramachandran outliers	138981	2580 (1.56-1.52)
Sidechain outliers	138945	2577(1.56-1.52)
RSRZ outliers	127900	2524 (1.56-1.52)

The table below summarises the geometric issues observed across the polymeric chains and their fit to the electron density. The red, orange, yellow and green segments on the lower bar indicate the fraction of residues that contain outliers for >=3, 2, 1 and 0 types of geometric quality criteria respectively. A grey segment represents the fraction of residues that are not modelled. The numeric value for each fraction is indicated below the corresponding segment, with a dot representing fractions <=5% The upper red bar (where present) indicates the fraction of residues that have poor fit to the electron density. The numeric value is given above the bar.

Mol	Chain	Length	Quality of chain	
1	А	157	94%	• •
1	В	157	% 	• 10%
2	С	18	83%	11% 6%
2	D	18	100%	



2 Entry composition (i)

There are 3 unique types of molecules in this entry. The entry contains 5727 atoms, of which 2686 are hydrogens and 0 are deuteriums.

In the tables below, the ZeroOcc column contains the number of atoms modelled with zero occupancy, the AltConf column contains the number of residues with at least one atom in alternate conformation and the Trace column contains the number of residues modelled with at most 2 atoms.

• Molecule 1 is a protein called Induced myeloid leukemia cell differentiation protein Mcl-1.

Mol	Chain	Residues		Atoms						AltConf	Trace
1	1 A 154	Total	С	Η	Ν	Ο	S	0	2	0	
		104	2506	780	1263	231	228	4	0	5	0
1	В	141	Total	С	Η	Ν	Ο	S	0	2	0
	D	T.T.T	2314	724	1165	212	210	3	0		

There are 2 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
А	171	GLY	-	EXPRESSION TAG	UNP Q07820
В	171	GLY	-	EXPRESSION TAG	UNP Q07820

• Molecule 2 is a protein called Mcl-1 BH3 peptide.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
2	С	18	Total	С	Η	Ν	Ο	Ο	0	1
		10	260	77	129	30	24	0		
0	а	18	Total	С	Η	Ν	Ο	0	0	1
		10	260	77	129	30	24	0		

• Molecule 3 is water.

Mol	Chain	Residues	Atoms	ZeroOcc	AltConf
3	А	212	Total O 212 212	0	0
3	В	119	Total O 119 119	0	0
3	С	32	$\begin{array}{cc} \text{Total} & \text{O} \\ 32 & 32 \end{array}$	0	0
3	D	24	Total O 24 24	0	0



3 Residue-property plots (i)

These plots are drawn for all protein, RNA and DNA chains in the entry. The first graphic for a chain summarises the proportions of the various outlier classes displayed in the second graphic. The second graphic shows the sequence view annotated by issues in geometry and electron density. Residues are color-coded according to the number of geometric quality criteria for which they contain at least one outlier: green = 0, yellow = 1, orange = 2 and red = 3 or more. A red dot above a residue indicates a poor fit to the electron density (RSRZ > 2). Stretches of 2 or more consecutive residues without any outlier are shown as a green connector. Residues present in the sample, but not in the model, are shown in grey.

• Molecule 1: Induced myeloid leukemia cell differentiation protein Mcl-1

Chain A:	94%	• •
6171 4190 1214 1214 12218 12218 12218 1228 1228 1		
• Molecule 1: Induced myeloid leuk	cemia cell differentiation protei	n Mcl-1
Chain B:	85%	• 10%
C171 D172 D172 D172 C192 C192 C192 C192 C192 C203 C203 C203 C203 C203 C203 C203 C20	ALLA CLY CLY CLY	
• Molecule 2: Mcl-1 BH3 peptide		
Chain C:	83%	11% 6%
N N N N N N N N N N N N N N N N N N N		
• Molecule 2: Mcl-1 BH3 peptide		
Chain D:	100%	

There are no outlier residues recorded for this chain.



4 Data and refinement statistics (i)

Property	Value	Source
Space group	P 1 21 1	Depositor
Cell constants	50.07Å 48.35 Å 68.18 Å	Depositor
a, b, c, α , β , γ	90.00° 93.83° 90.00°	Depositor
Resolution (Å)	34.74 - 1.53	Depositor
Resolution (A)	49.96 - 1.53	EDS
% Data completeness	99.9 (34.74 - 1.53)	Depositor
(in resolution range)	$99.9 \ (49.96 - 1.53)$	EDS
R _{merge}	0.05	Depositor
R_{sym}	0.04	Depositor
$< I/\sigma(I) > 1$	$2.75 (at 1.53 \text{\AA})$	Xtriage
Refinement program	PHENIX (phenix.refine: 1.8_1069)	Depositor
B B.	0.137 , 0.184	Depositor
R, R_{free}	0.138 , 0.183	DCC
R _{free} test set	2495 reflections $(5.06%)$	wwPDB-VP
Wilson B-factor $(Å^2)$	17.1	Xtriage
Anisotropy	0.629	Xtriage
Bulk solvent $k_{sol}(e/Å^3), B_{sol}(Å^2)$	0.41 , 53.0	EDS
L-test for twinning ²	$< L >=0.49, < L^2>=0.32$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
F_o, F_c correlation	0.98	EDS
Total number of atoms	5727	wwPDB-VP
Average B, all atoms $(Å^2)$	21.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: The largest off-origin peak in the Patterson function is 8.81% of the height of the origin peak. No significant pseudotranslation is detected.

²Theoretical values of $\langle |L| \rangle$, $\langle L^2 \rangle$ for acentric reflections are 0.5, 0.333 respectively for untwinned datasets, and 0.375, 0.2 for perfectly twinned datasets.



¹Intensities estimated from amplitudes.

5 Model quality (i)

5.1 Standard geometry (i)

Bond lengths and bond angles in the following residue types are not validated in this section: ACE, $\rm NH2$

The Z score for a bond length (or angle) is the number of standard deviations the observed value is removed from the expected value. A bond length (or angle) with |Z| > 5 is considered an outlier worth inspection. RMSZ is the root-mean-square of all Z scores of the bond lengths (or angles).

Mol	Chain	Bond	lengths	Bond angles		
	Chain	RMSZ	# Z > 5	RMSZ	# Z > 5	
1	А	0.46	0/1272	0.58	0/1710	
1	В	0.38	0/1173	0.49	0/1576	
2	С	0.45	0/128	1.13	2/171~(1.2%)	
2	D	0.45	0/128	0.69	0/171	
All	All	0.43	0/2701	0.59	2/3628~(0.1%)	

There are no bond length outliers.

All (2) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	$\mathbf{Observed}(^{o})$	$Ideal(^{o})$
2	С	0	ACE	O-C-N	10.55	139.57	122.70
2	С	0	ACE	C-N-CA	6.61	138.22	121.70

There are no chirality outliers.

There are no planarity outliers.

5.2 Too-close contacts (i)

In the following table, the Non-H and H(model) columns list the number of non-hydrogen atoms and hydrogen atoms in the chain respectively. The H(added) column lists the number of hydrogen atoms added and optimized by MolProbity. The Clashes column lists the number of clashes within the asymmetric unit, whereas Symm-Clashes lists symmetry related clashes.

Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
1	А	1243	1263	1253	6	0
1	В	1149	1165	1161	9	0
2	С	131	129	131	4	0
2	D	131	129	131	0	0
3	А	212	0	0	5	1

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Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes		
3	В	119	0	0	6	1		
3	С	32	0	0	1	1		
3	D	24	0	0	0	1		
All	All	3041	2686	2676	20	2		

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The all-atom clashscore is defined as the number of clashes found per 1000 atoms (including hydrogen atoms). The all-atom clashscore for this structure is 4.

All (20) close contacts within the same asymmetric unit are listed below, sorted by their clash magnitude.

Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:A:281:ILE:O	3:A:607:HOH:O	1.82	0.96
1:B:250:MET:SD	3:B:494:HOH:O	2.31	0.87
1:B:191:THR:C	3:B:518:HOH:O	2.17	0.81
1:B:191:THR:O	3:B:518:HOH:O	2.01	0.77
2:C:0:ACE:H3	3:C:131:HOH:O	1.85	0.76
1:B:203:GLY:N	3:B:498:HOH:O	2.25	0.69
1:B:191:THR:OG1	1:B:192:GLY:N	2.27	0.67
1:B:192:GLY:HA2	3:B:485:HOH:O	1.96	0.65
1:B:203:GLY:O	3:B:492:HOH:O	2.14	0.65
2:C:0:ACE:H2	2:C:4:THR:H	1.74	0.53
1:A:277:HIS:HD2	3:A:523:HOH:O	1.94	0.50
1:B:172:ASP:OD2	1:B:303:ARG:NH2	2.43	0.50
1:A:277:HIS:CD2	3:A:523:HOH:O	2.66	0.48
2:C:0:ACE:CH3	2:C:4:THR:H	2.26	0.48
1:A:283:GLN:HG2	3:A:607:HOH:O	2.14	0.47
1:A:190:ALA:O	1:A:279:LYS:HD3	2.17	0.45
1:B:299:VAL:O	1:B:303:ARG:HB2	2.16	0.45
2:C:0:ACE:H2	2:C:1:ALA:C	2.39	0.43
1:A:214:ARG:O	1:A:218:ASP:HB2	2.20	0.42

All (2) symmetry-related close contacts are listed below. The label for Atom-2 includes the symmetry operator and encoded unit-cell translations to be applied.

Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
3:B:515:HOH:O	3:D:124:HOH:O[2_454]	1.45	0.75
3:A:575:HOH:O	3:C:116:HOH:O[2_455]	1.81	0.39



5.3 Torsion angles (i)

5.3.1 Protein backbone (i)

In the following table, the Percentiles column shows the percent Ramachandran outliers of the chain as a percentile score with respect to all X-ray entries followed by that with respect to entries of similar resolution.

The Analysed column shows the number of residues for which the backbone conformation was analysed, and the total number of residues.

Mol	Chain	Analysed	Favoured	Allowed	Outliers	Percentiles
1	А	155/157~(99%)	153~(99%)	2(1%)	0	100 100
1	В	139/157~(88%)	138~(99%)	1 (1%)	0	100 100
2	С	16/18~(89%)	16 (100%)	0	0	100 100
2	D	16/18~(89%)	16 (100%)	0	0	100 100
All	All	326/350~(93%)	323~(99%)	3~(1%)	0	100 100

There are no Ramachandran outliers to report.

5.3.2 Protein sidechains (i)

In the following table, the Percentiles column shows the percent sidechain outliers of the chain as a percentile score with respect to all X-ray entries followed by that with respect to entries of similar resolution.

The Analysed column shows the number of residues for which the sidechain conformation was analysed, and the total number of residues.

Mol	Chain	Analysed	Rotameric	Outliers	Percentiles
1	А	134/135~(99%)	134~(100%)	0	100 100
1	В	125/135~(93%)	125~(100%)	0	100 100
2	С	13/13~(100%)	13~(100%)	0	100 100
2	D	13/13~(100%)	13~(100%)	0	100 100
All	All	285/296~(96%)	285~(100%)	0	100 100

There are no protein residues with a non-rotameric sidechain to report.

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (3) such sidechains are listed below:



Mol	Chain	Res	Type
1	В	252	HIS
2	С	16	HIS
2	D	16	HIS

5.3.3 RNA (i)

There are no RNA molecules in this entry.

5.4 Non-standard residues in protein, DNA, RNA chains (i)

There are no non-standard protein/DNA/RNA residues in this entry.

5.5 Carbohydrates (i)

There are no carbohydrates in this entry.

5.6 Ligand geometry (i)

There are no ligands in this entry.

5.7 Other polymers (i)

There are no such residues in this entry.

5.8 Polymer linkage issues (i)

There are no chain breaks in this entry.



6 Fit of model and data (i)

6.1 Protein, DNA and RNA chains (i)

In the following table, the column labelled '#RSRZ> 2' contains the number (and percentage) of RSRZ outliers, followed by percent RSRZ outliers for the chain as percentile scores relative to all X-ray entries and entries of similar resolution. The OWAB column contains the minimum, median, 95^{th} percentile and maximum values of the occupancy-weighted average B-factor per residue. The column labelled 'Q< 0.9' lists the number of (and percentage) of residues with an average occupancy less than 0.9.

Mol	Chain	Analysed	<RSRZ $>$	# RSRZ > 2	$OWAB(Å^2)$	$Q{<}0.9$
1	А	154/157~(98%)	-0.57	0 100 100	7, 13, 27, 47	0
1	В	141/157~(89%)	-0.41	2 (1%) 75 79	10, 20, 42, 54	0
2	С	16/18~(88%)	-0.52	0 100 100	10, 11, 22, 28	0
2	D	16/18~(88%)	-0.71	0 100 100	11, 14, 22, 28	0
All	All	327/350~(93%)	-0.50	2 (0%) 89 91	7, 16, 35, 54	0

All (2) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	В	171	GLY	5.8
1	В	192	GLY	2.8

6.2 Non-standard residues in protein, DNA, RNA chains (i)

There are no non-standard protein/DNA/RNA residues in this entry.

6.3 Carbohydrates (i)

There are no carbohydrates in this entry.

6.4 Ligands (i)

There are no ligands in this entry.

6.5 Other polymers (i)

There are no such residues in this entry.

